Ranavirus SIR Model

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Texas Tech University

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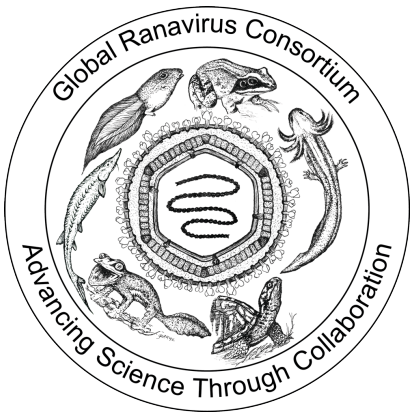
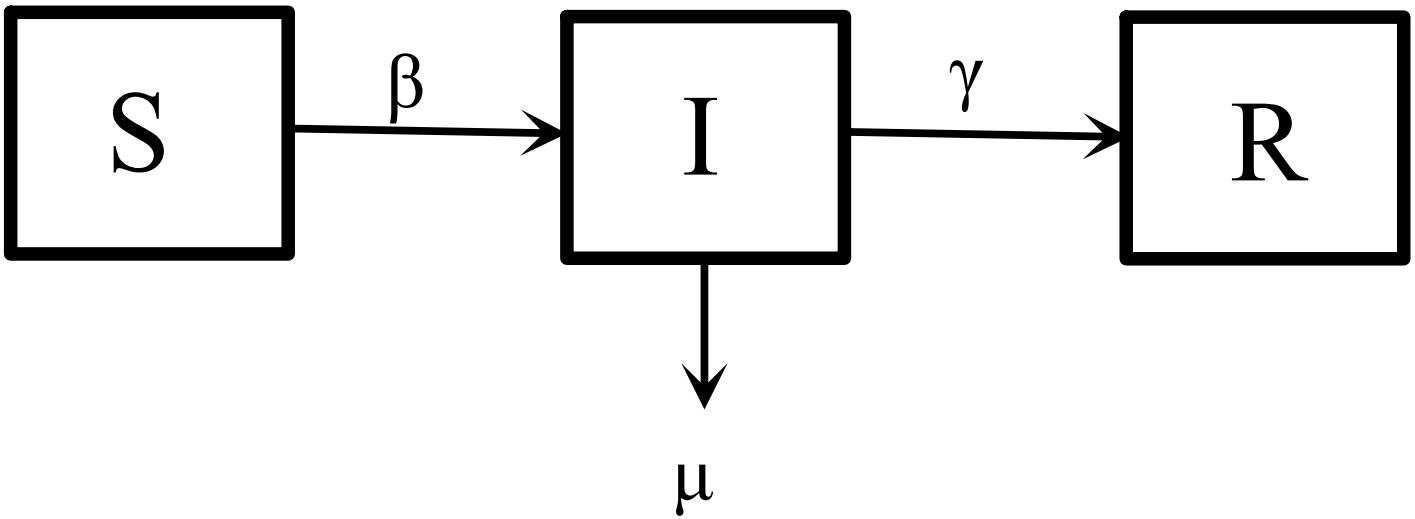
Global Ranavirus Consortium Course



Outline

- Review basic SIR differential equations model
- Formulate model for Ranavirus
  - direct transmission
  - environmental transmission
  - necrophagy transmission
- Parameterize model
  - Possible due to lots of work done by: Suzanne O'Regan, Jennifer A. Spatz, Patrick N. Reilly, Rachel D. Hill, E. Davis Carter, Rebecca P. Wilkes, Debra L. Miller, Matt Gray
- Model simulations
- Update model to be more realistic

Basic SIR Model review



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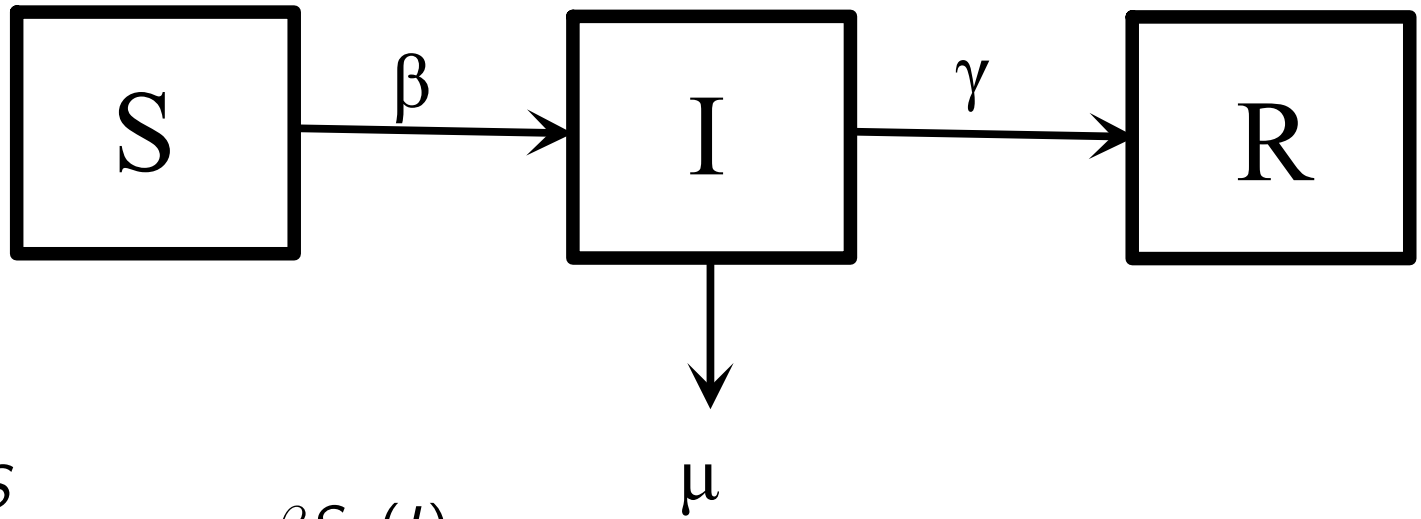
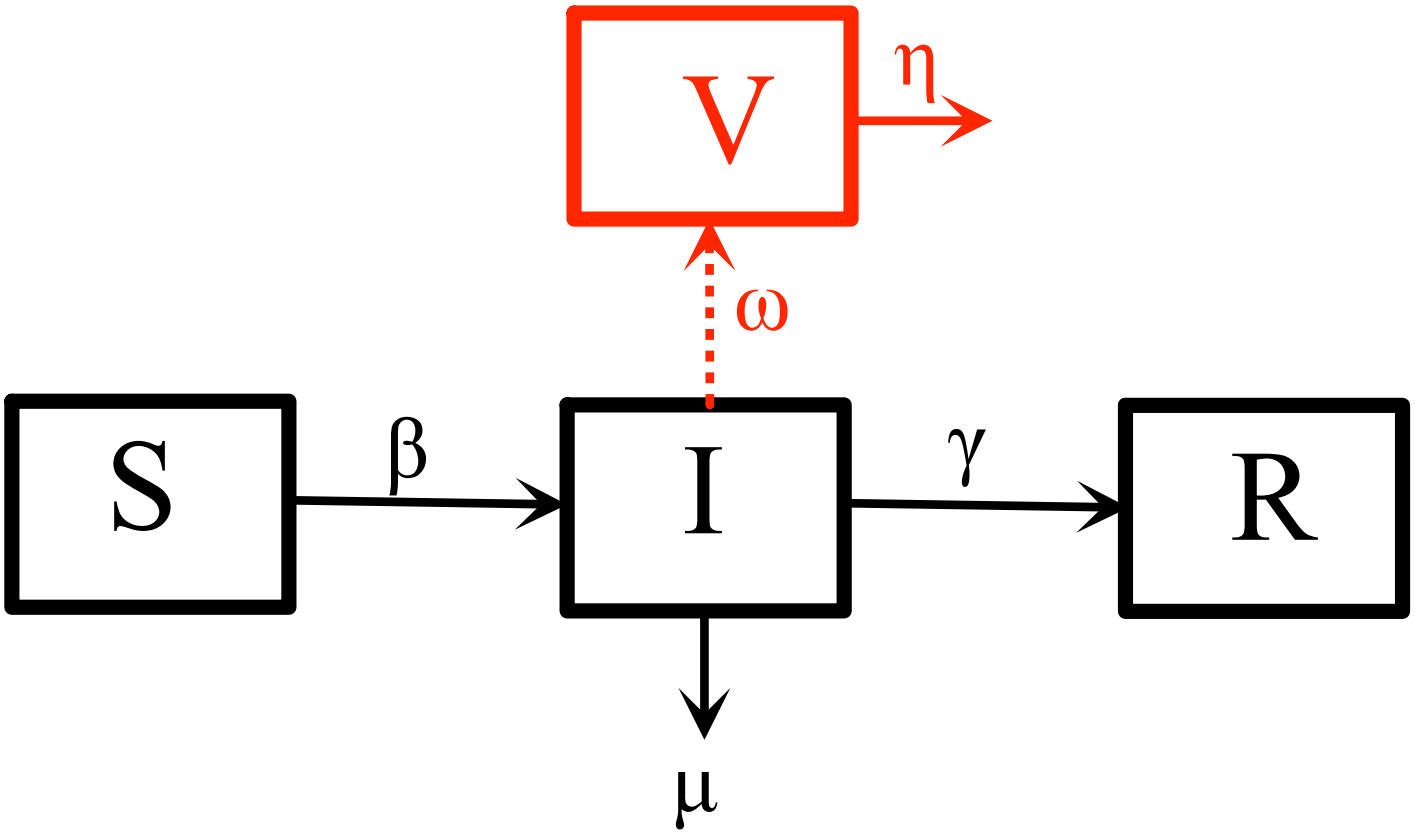


$$\frac{dS}{dt} = \underbrace{-\beta S g(I)}_{\text{direct transmission}}$$

$$\frac{dI}{dt} = \underbrace{\beta S g(I)}_{\text{direct transmission}} - \underbrace{\mu I}_{\text{disease induced death}} - \underbrace{\gamma I}_{\text{recovery}}$$

$$\frac{dR}{dt} = \underbrace{\gamma I}_{\text{recovery}}$$

Basic SIR Viral Model



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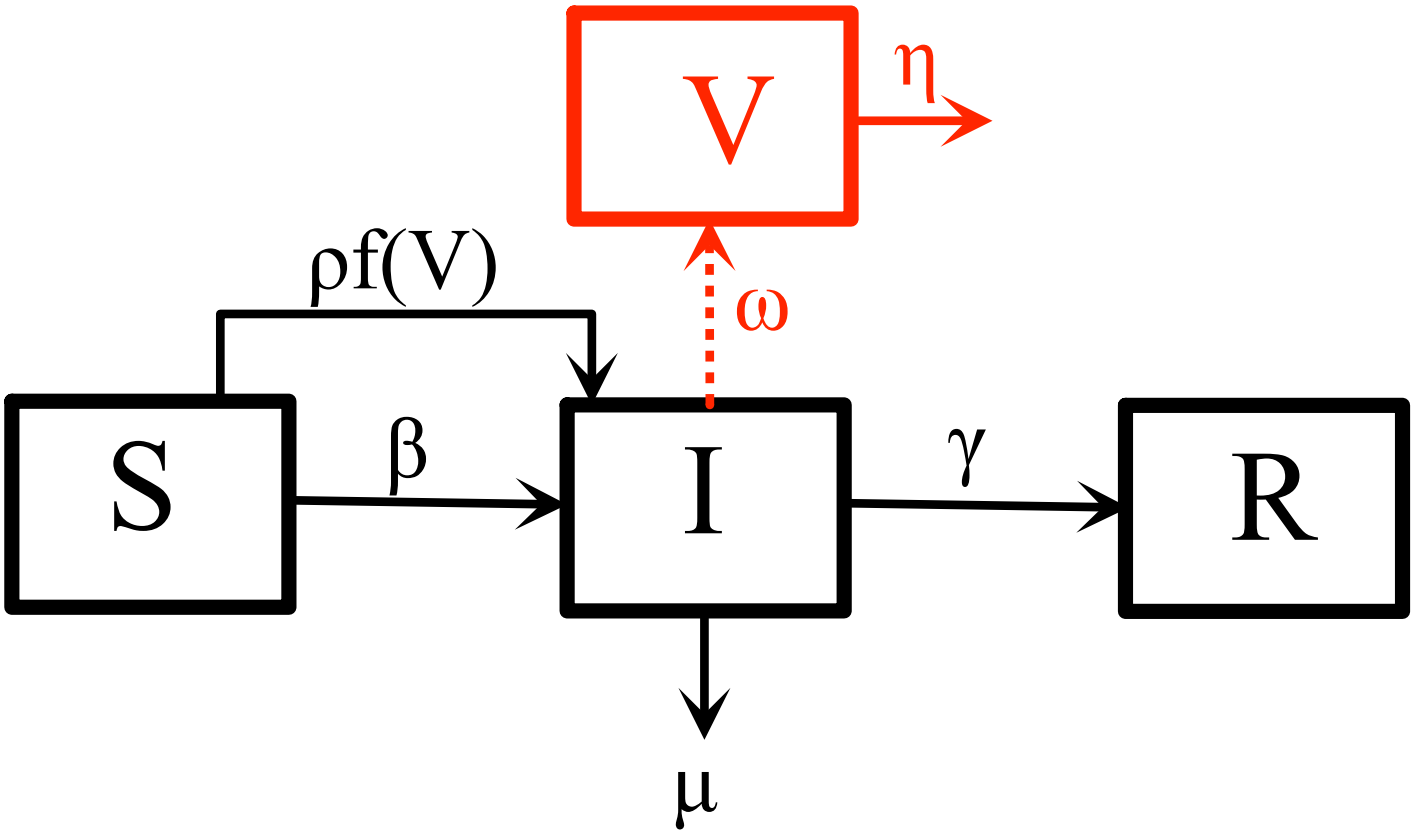

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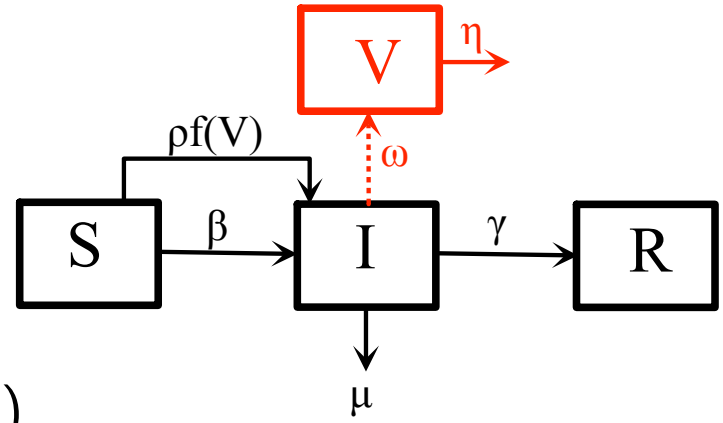

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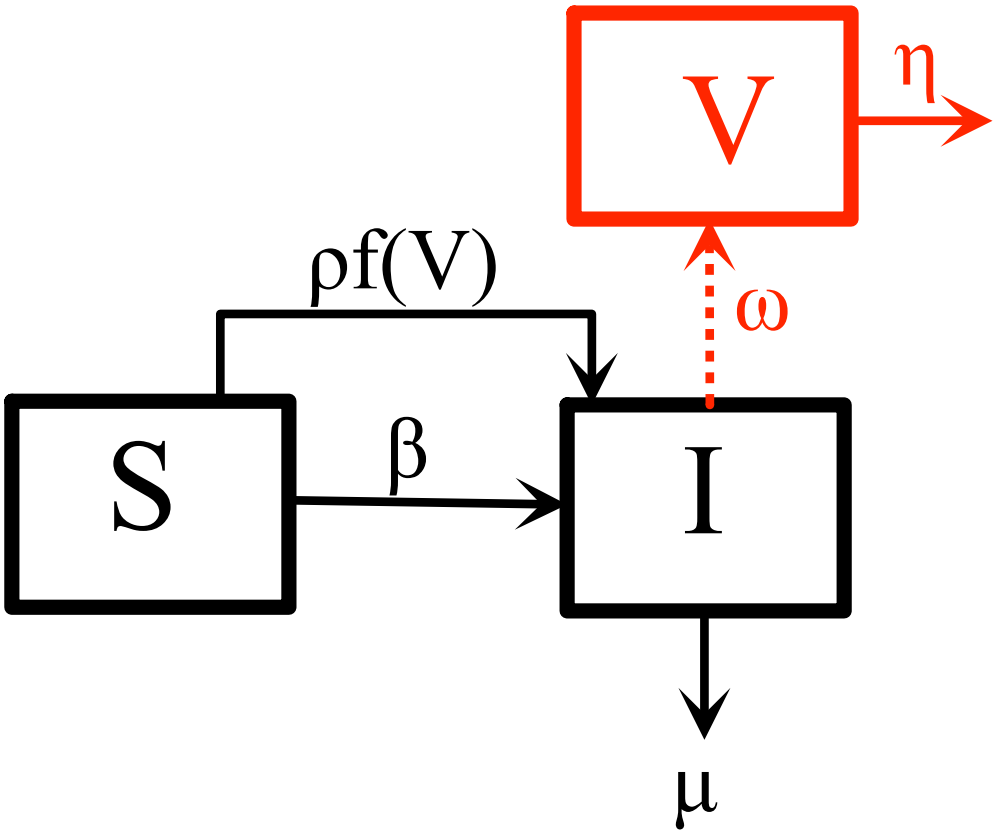
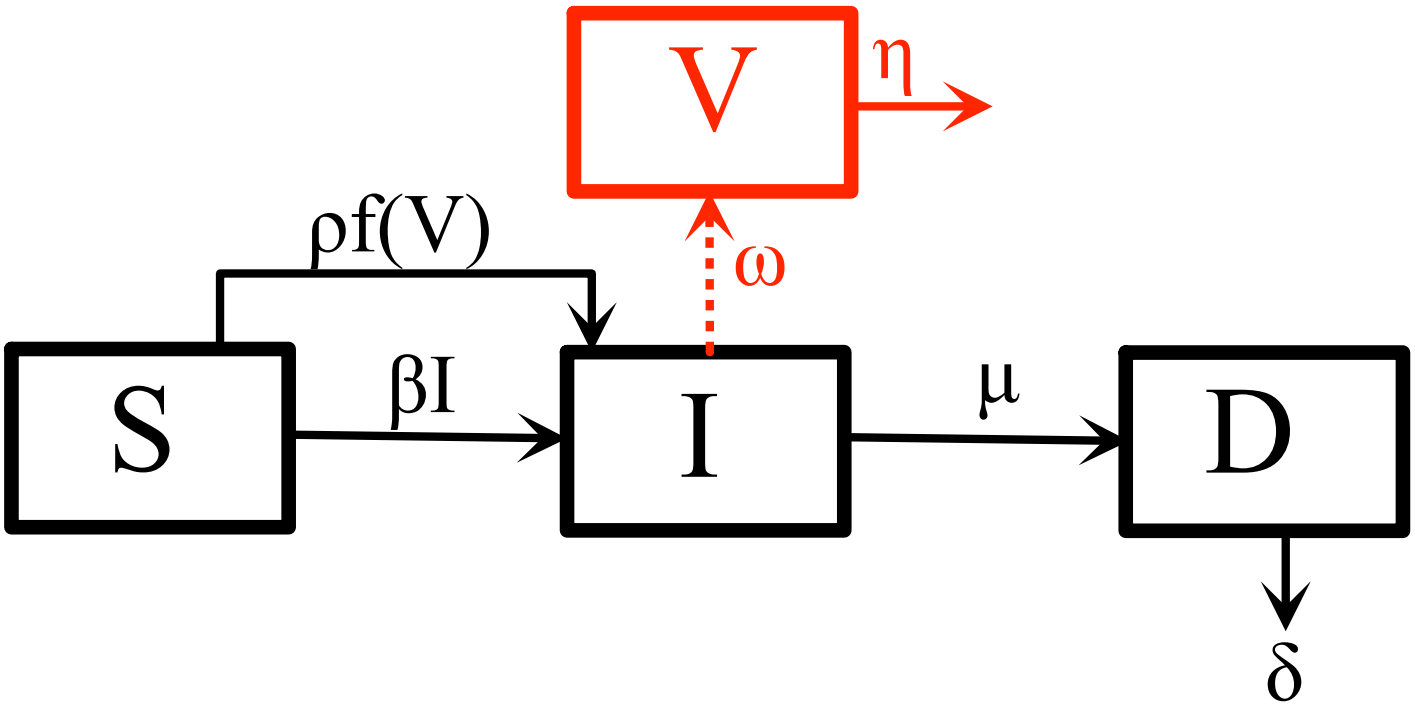
$$\frac{dR}{dt} = \underbrace{\gamma I}_{\text{recovery}}$$

$$\frac{dV}{dt} = \underbrace{\omega I}_{\text{shed virions}} - \underbrace{\eta V}_{\text{degradation}}$$

SI Viral Model without Recovery



SI Viral Model with Necrophagy



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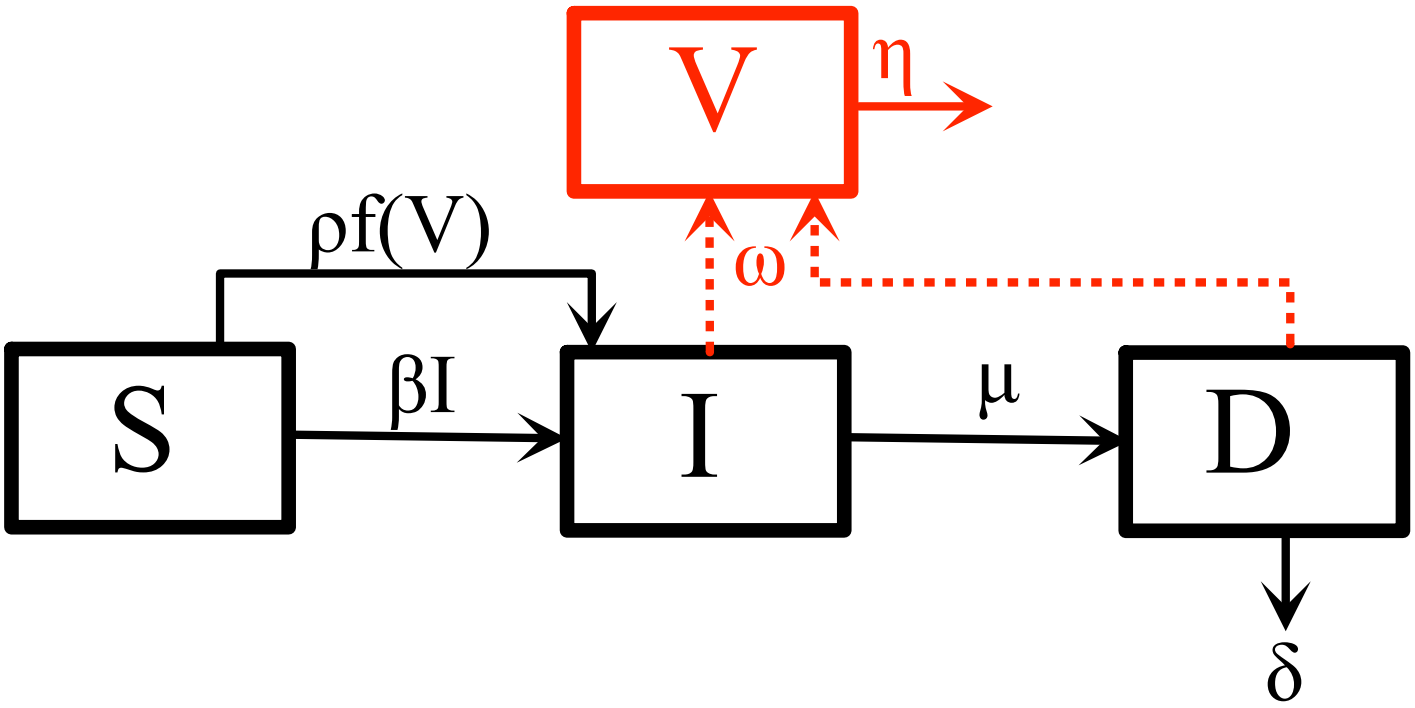

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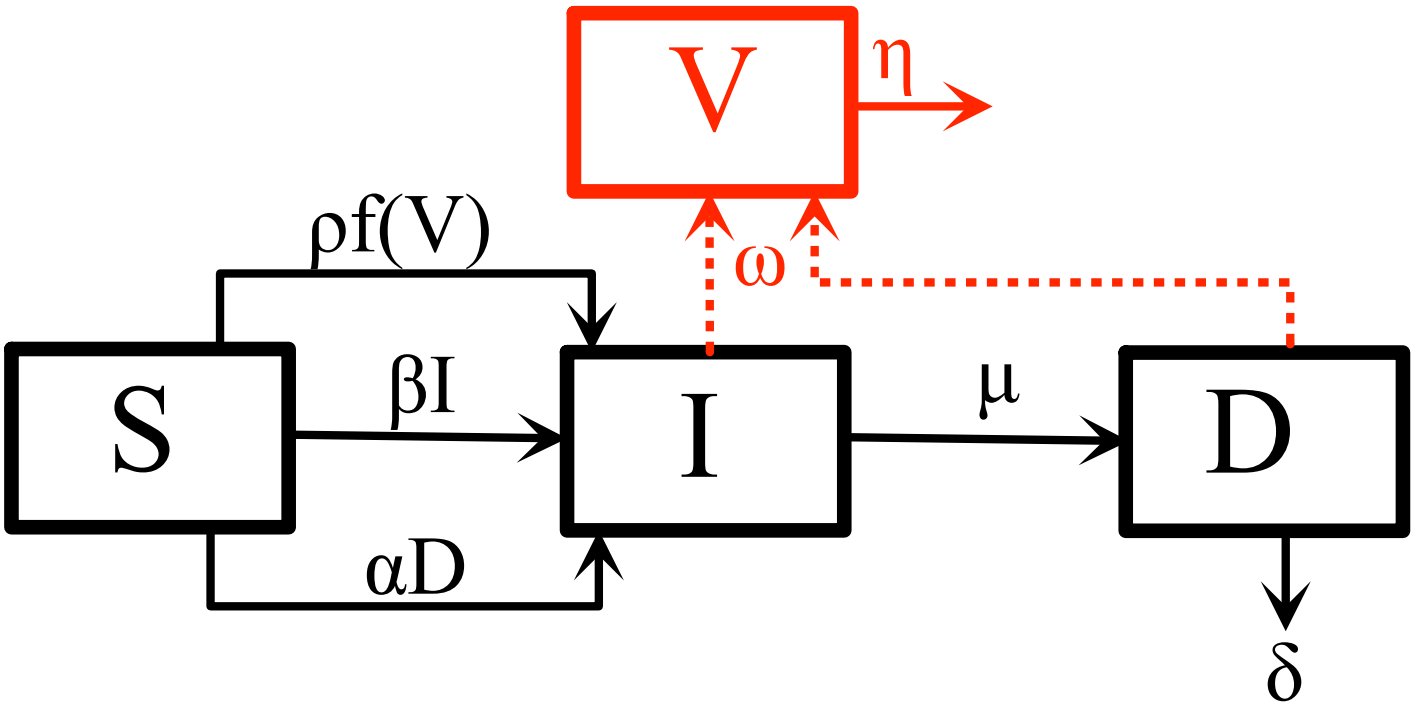

SI Viral Model with Necrophagy

$$\frac{dS}{dt} = \underbrace{-\beta S g(I)}_{\text{direct transmission}} - \underbrace{\rho S f(V)}_{\text{environmental transmission}} - \underbrace{\alpha S g(D)}_{\text{necrophagy transmission}}$$

$$\frac{dI}{dt} = \underbrace{\beta S g(I)}_{\text{direct transmission}} + \underbrace{\rho S f(V)}_{\text{environmental transmission}} + \underbrace{\alpha S g(D)}_{\text{necrophagy transmission}} - \underbrace{\mu I}_{\text{viral induced death}}$$

$$\frac{dD}{dt} = \underbrace{\mu I}_{\text{viral induced death}} - \underbrace{\delta D}_{\text{necrophagy}}$$

$$\frac{dV}{dt} = \underbrace{\omega[I + D]}_{\text{shed virions}} - \underbrace{\eta V}_{\text{degradation}}$$

Frequency-dependent vs density-dependent transmission

- frequency-dependent tranmission
- per-individual contact rate is independent of population density
- Total population: $N(t) = S(t) + I(t)$

$$g(I) = I/N(t)$$

- density-dependent transmission
- transmission scales with population density

$$g(I) = I$$

Environmental transmission

The environmental contact rate function takes the following form:

$$f(V) = \frac{V}{V + \kappa}$$

where κ is the ranavirus ID50

Parameterization

ϕ	probability of infection
c	contact rate
ρ	environmental contact rate
β	direct transmission rate $\beta = \phi c$
ω	virion shedding rate
μ	diseased induced mortality
κ	ID50
$1/\delta$	mean dead tadpole survival time
α	necrophagy transmission rate $\alpha = \phi c$
$1/\eta$	environmental virion persistence time

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We'll talk about parameterizing these values today based on recent empirical data.

Contact Rate Experiment

- 1 infected frog in a 12-L tub with 20 susceptible frog.
- monitored the number of contacts between infected frog with susceptible frogs over 10 minutes
- monitored at 2, 4, and 6 hours

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Parameter	Description	unit
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- average 12 contacts in 10 minutes $\Longrightarrow$ 1.2 contacts/min
- $c = 1728$ / day
- assume $\rho = 1728$ / day

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- 1 infected individual in 1L fresh water
- took water samples at 3, 6, 12, 24, 48 and 72 hours
- measured viral load

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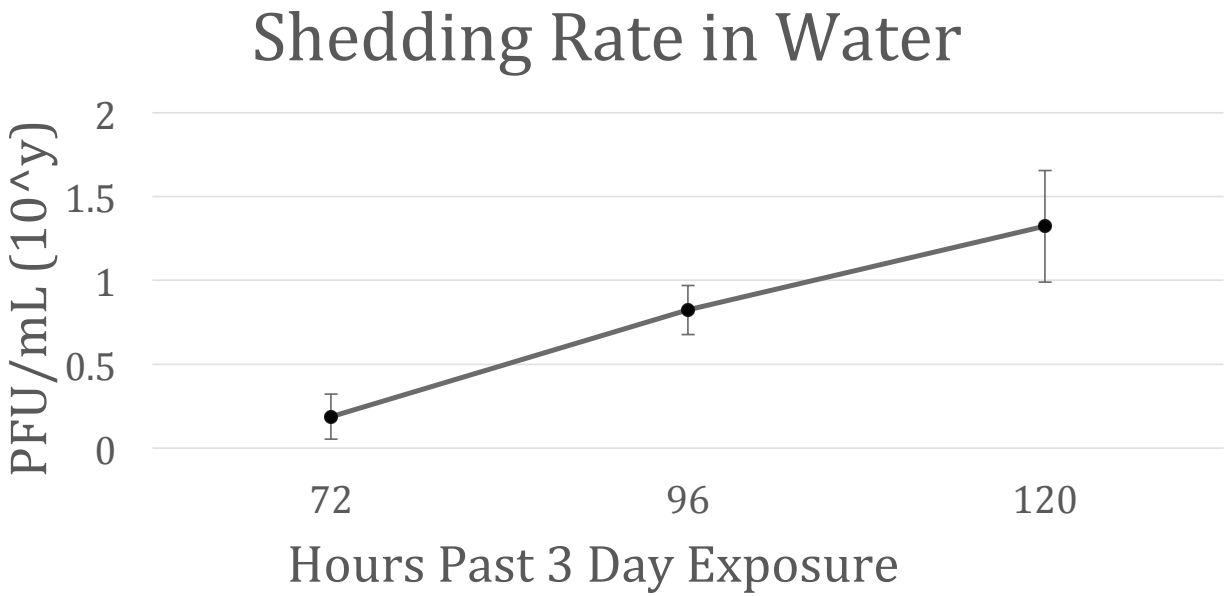
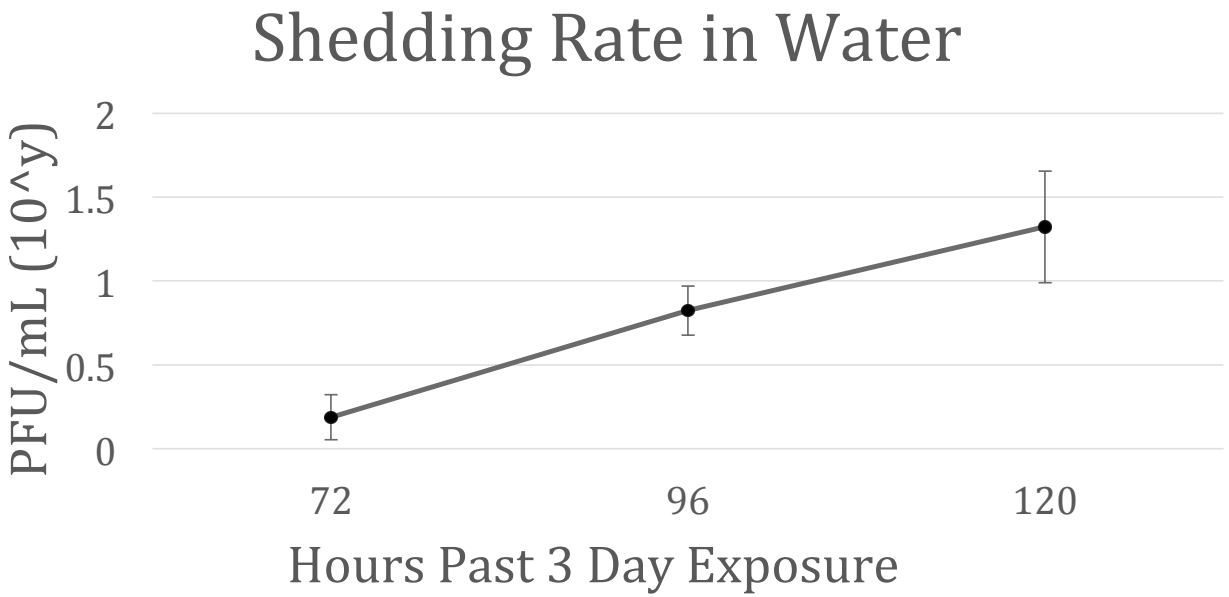


Shedding Rate Parameter



- Consider slope between 72 and 96 hours $= \frac{10^{0.8} - 10^{0.2} \text{ PFU/mL}}{24 \text{ hours}} = 5.11$
- Consider slope between 96 and 120 hours $= \frac{10^{1.3} - 10^{0.8} \text{ PFU/mL}}{24 \text{ hours}} = 14.36$
- Average these 2 values to get $\omega = 9.97$ PFU/mL/day/individual

Disease Induced Mortality Parameter

- Experiment: 1 infected frog (exposed 96 hours ago)
- Contact with Susceptible frogs
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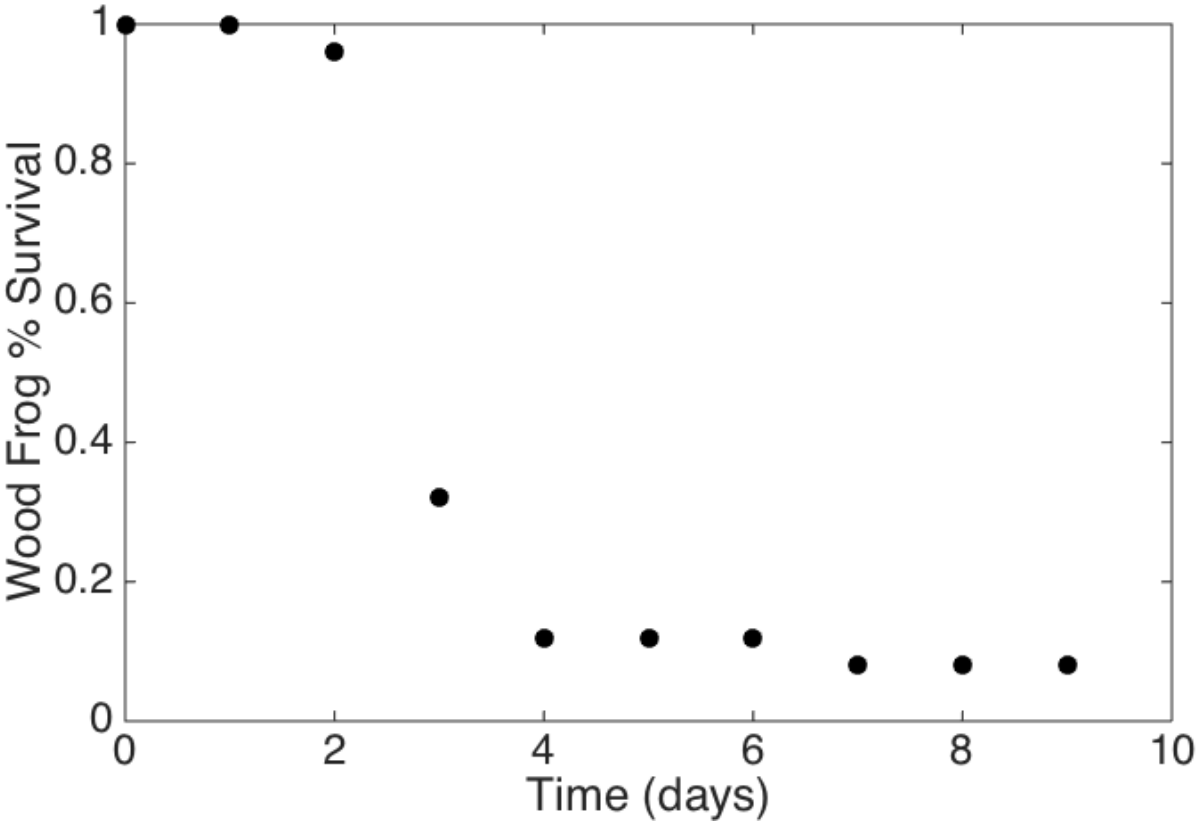

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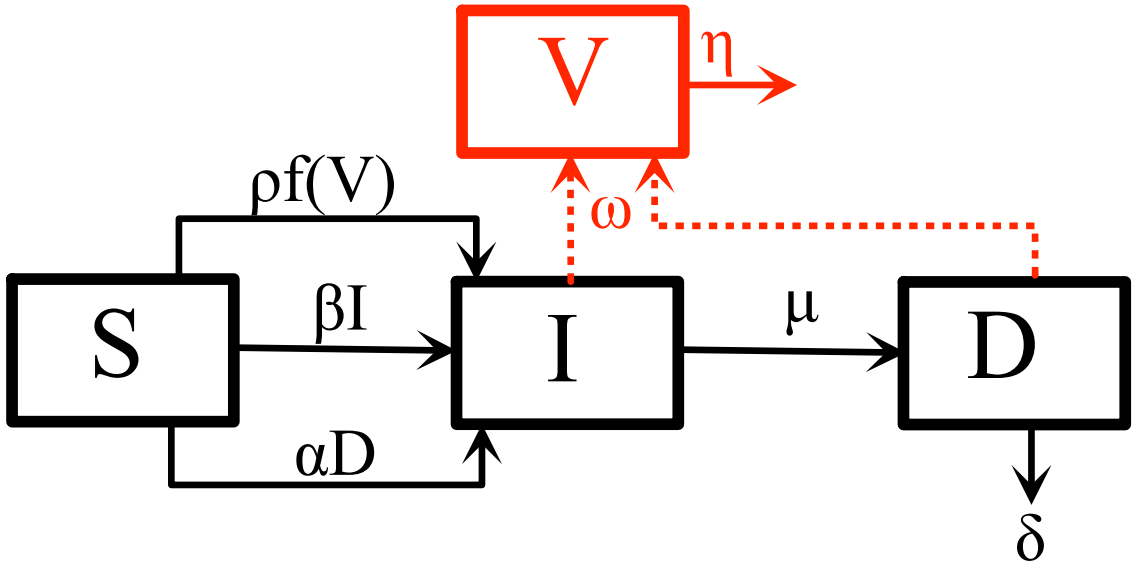
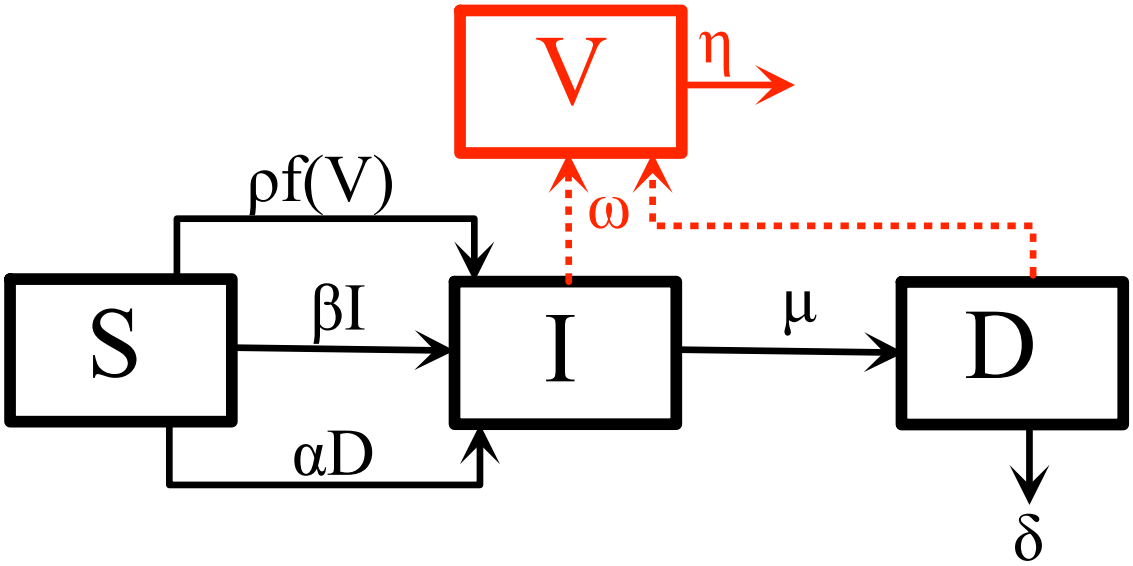


- $\mu =$ disease induced mortality

Disease Induced Mortality Parameter



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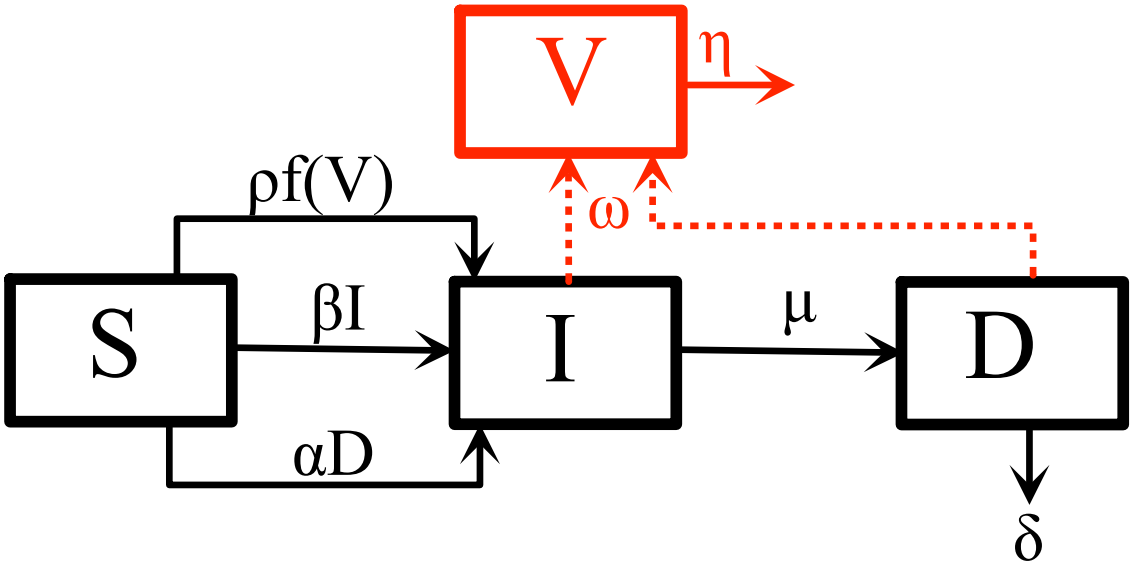
- $\frac{1}{\mu}$ = length of infection period

Disease Induced Mortality Parameter



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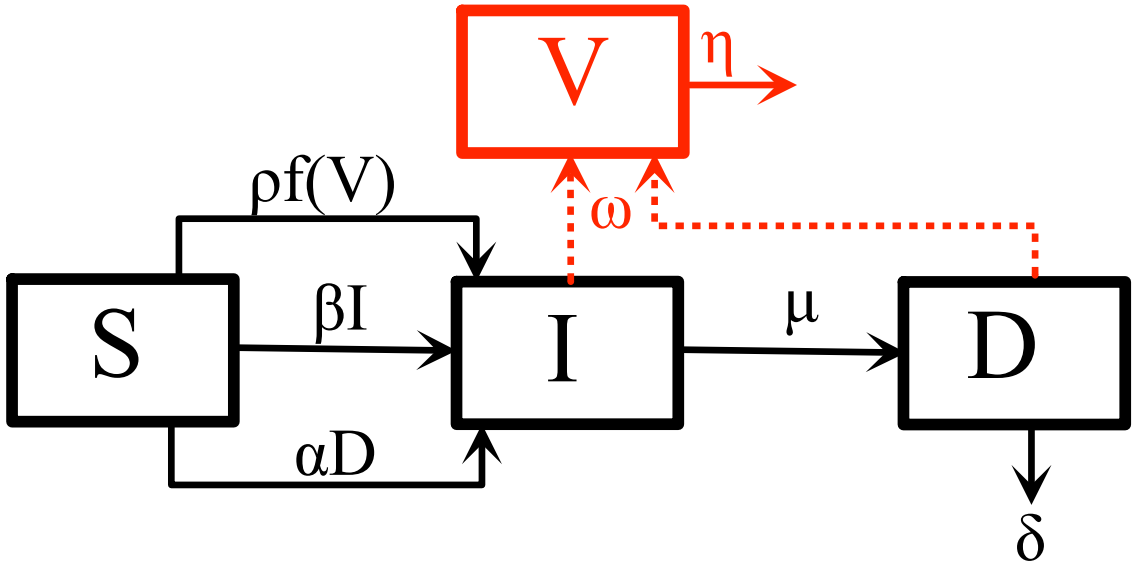
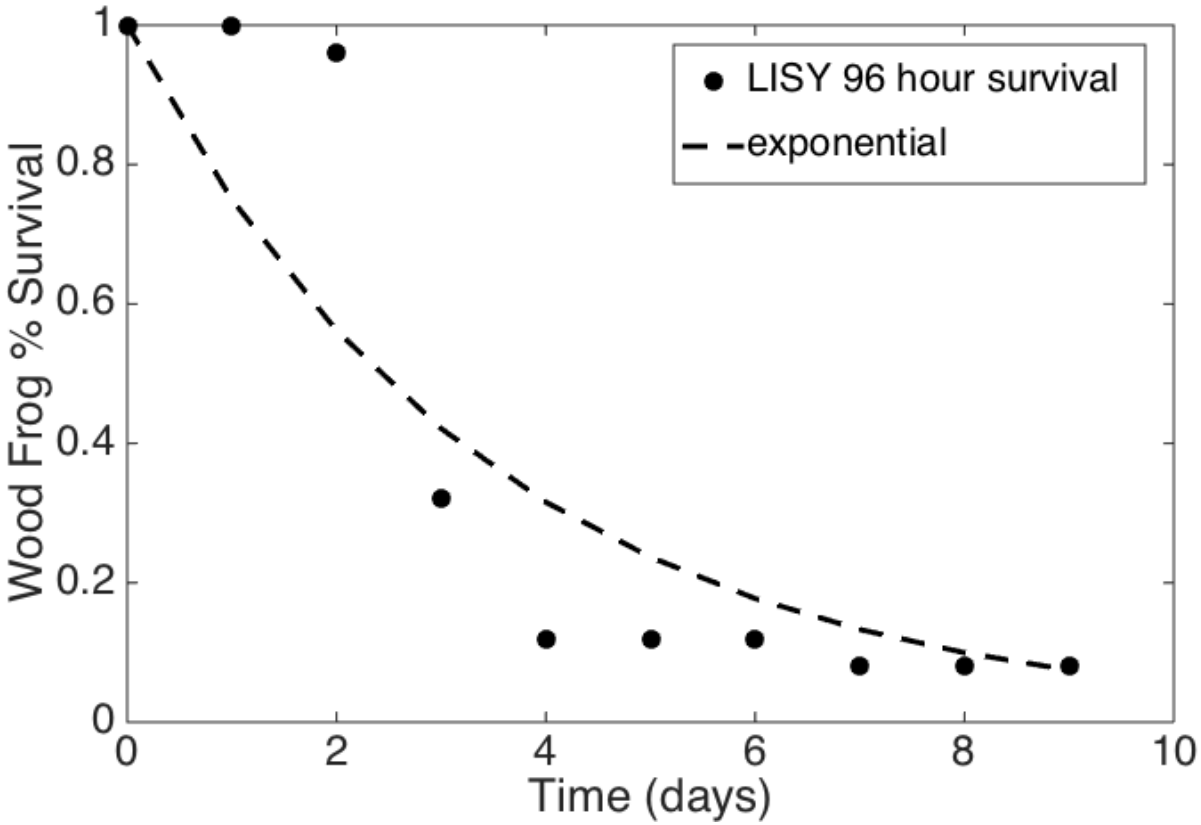


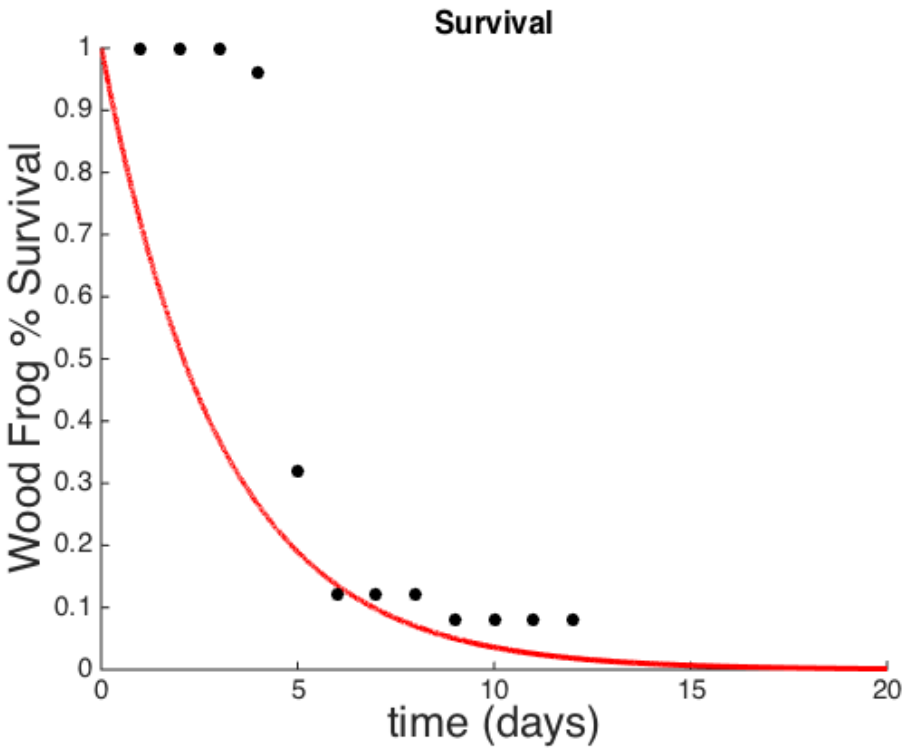
- μ = disease induced mortality
- $\frac{1}{\mu}$ = length of infection period
- Above model assumes this is exponentially distributed
- This means μ is constant and does not depend on the time spent in the compartment
  - ie: A frog that has been infected for 1 day is just as likely to die as a frog that has been infected for 3 days.
  - A unrealistic assumption of the model!

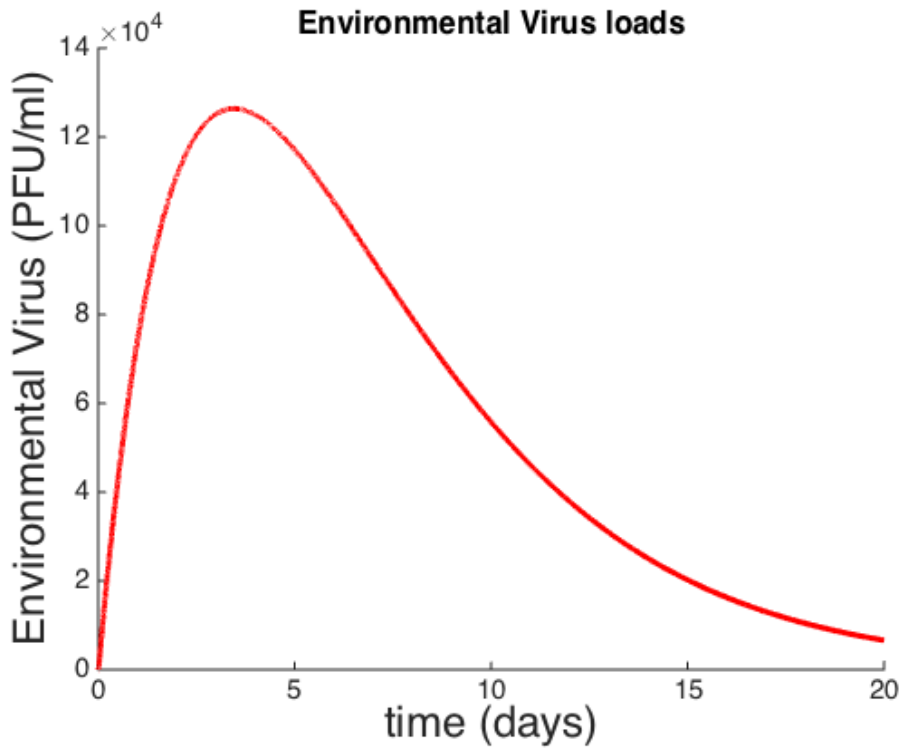
Disease Induced Mortality Parameter



Fit exponential function $y = e^{-\mu t}$

Model Simulations





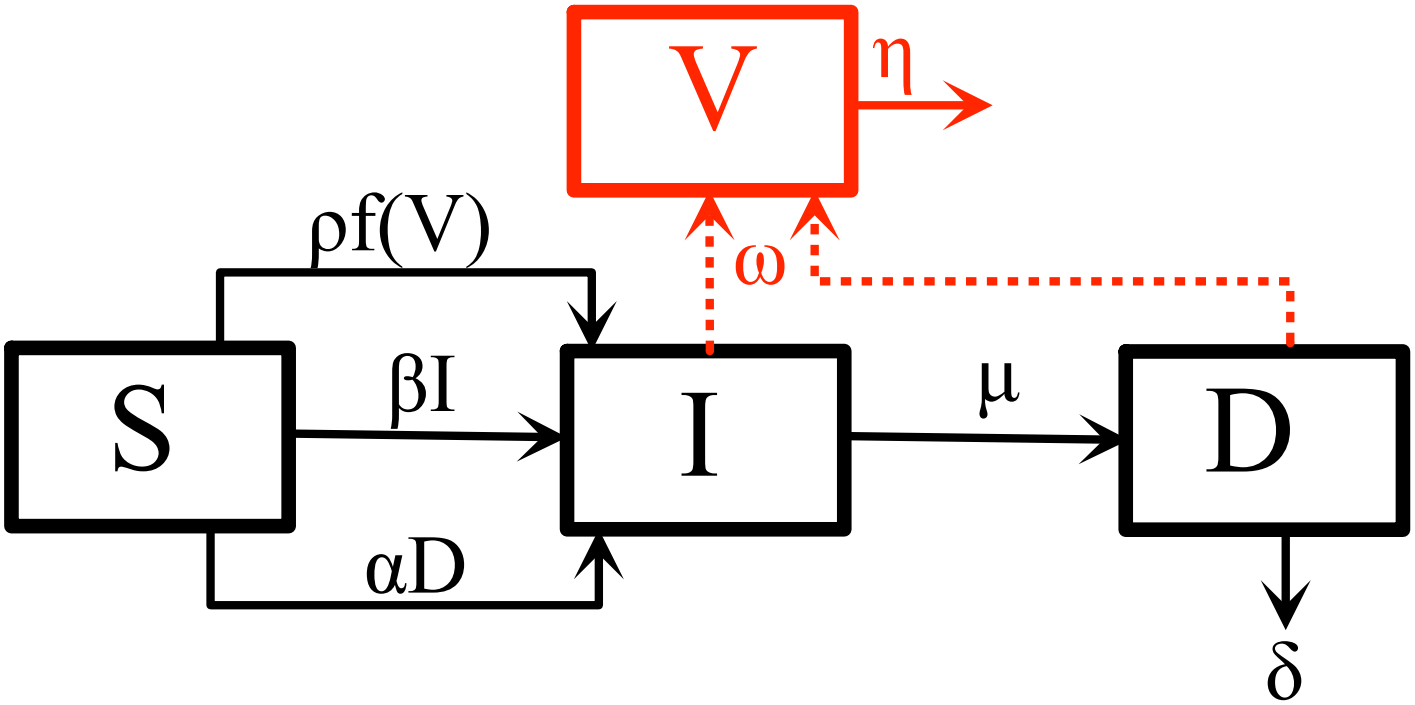
Update Model

- Add in a Latent compartment
  - A frog exposed to the virus isn't immediately infectious

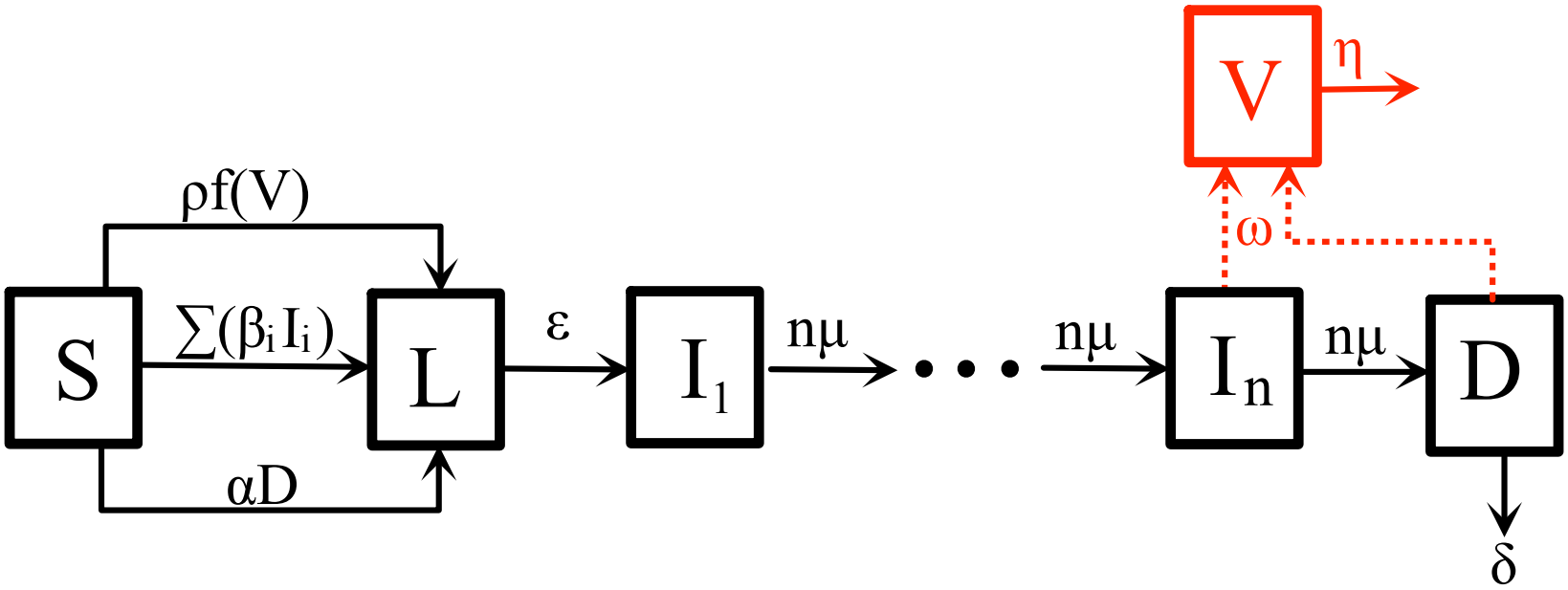
Update Model

- Add in a Latent compartment
  - A frog exposed to the virus isn't immediately infectious
- Consider a gamma distribution for mortality
  - probability of mortality increases the longer the individual resides in the infection class
  - Can achieve this by adding in stages of infection (multiple I compartments)
  - This works because the sum of a sequence of independent exponentially-distributed random variables is gamma-distributed

Base Model

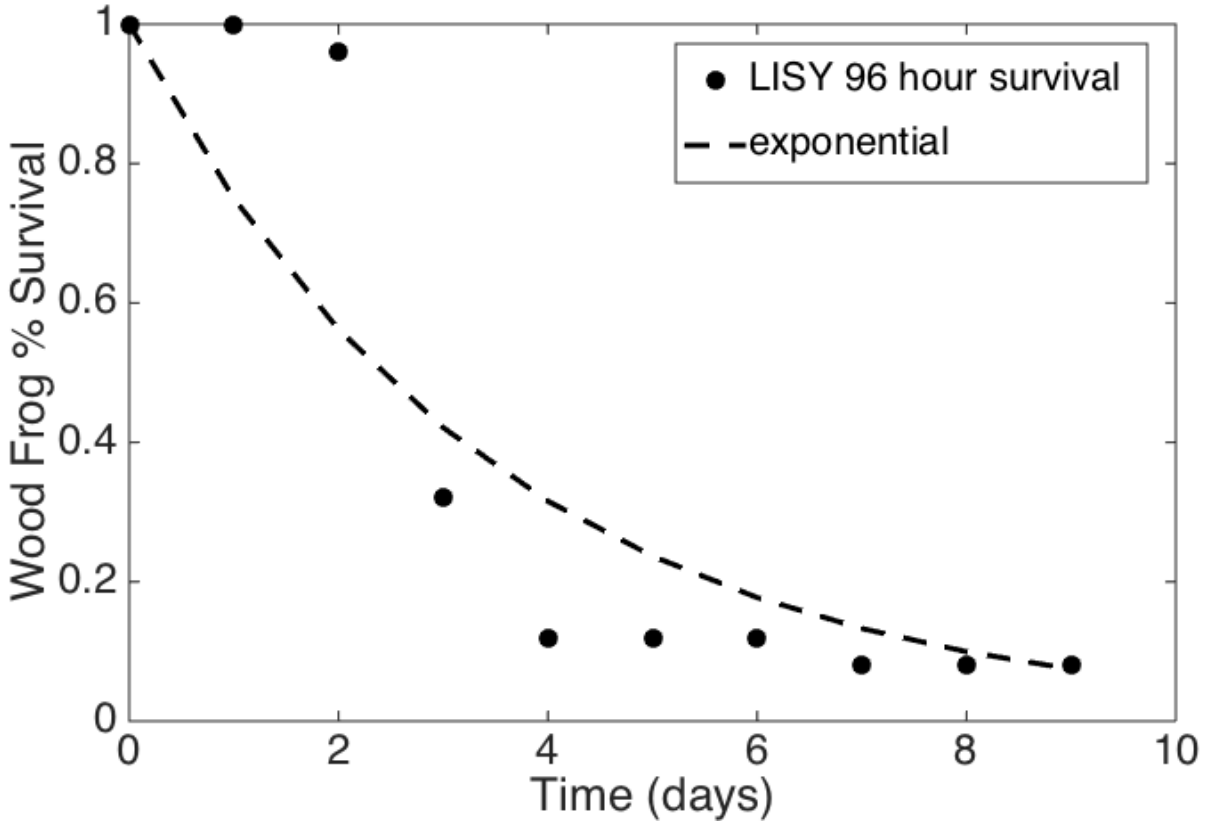


Full Model



Full Model: Disease Induced Mortality Parameter

μ	diseased induced mortality



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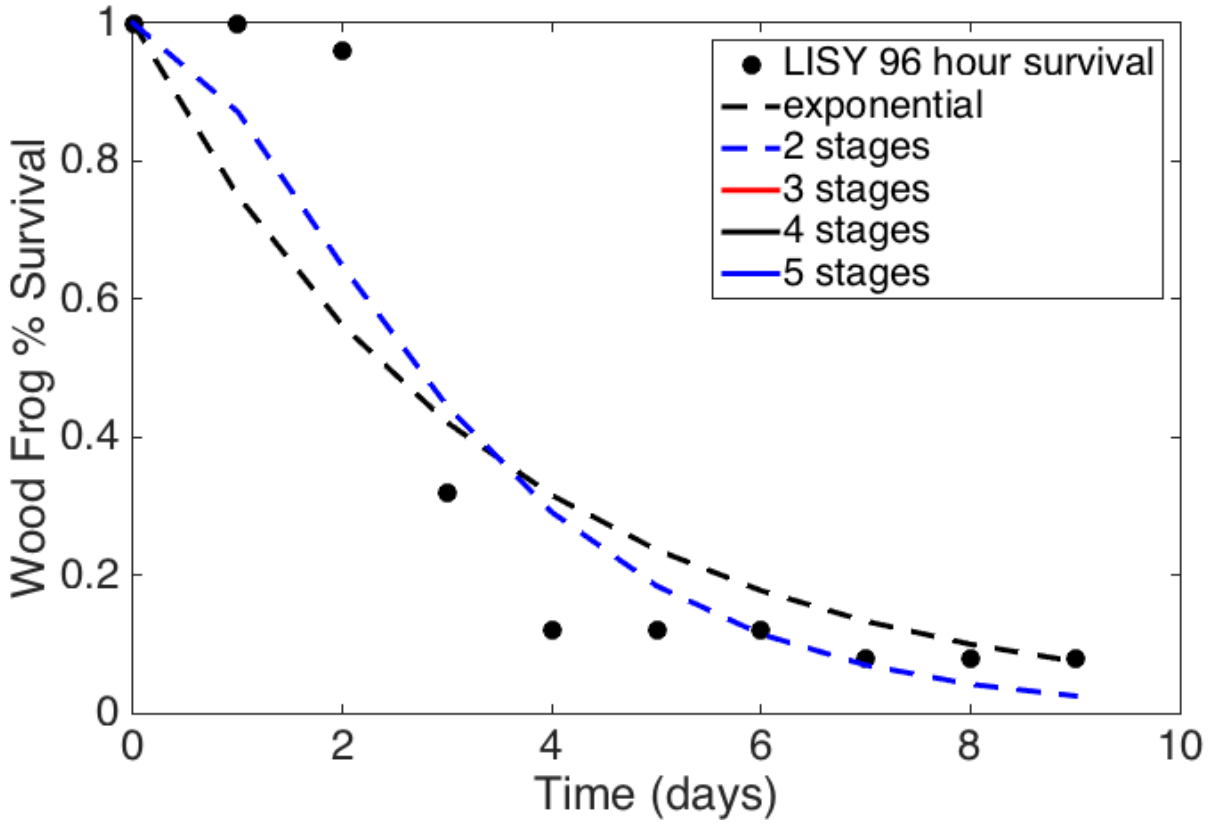

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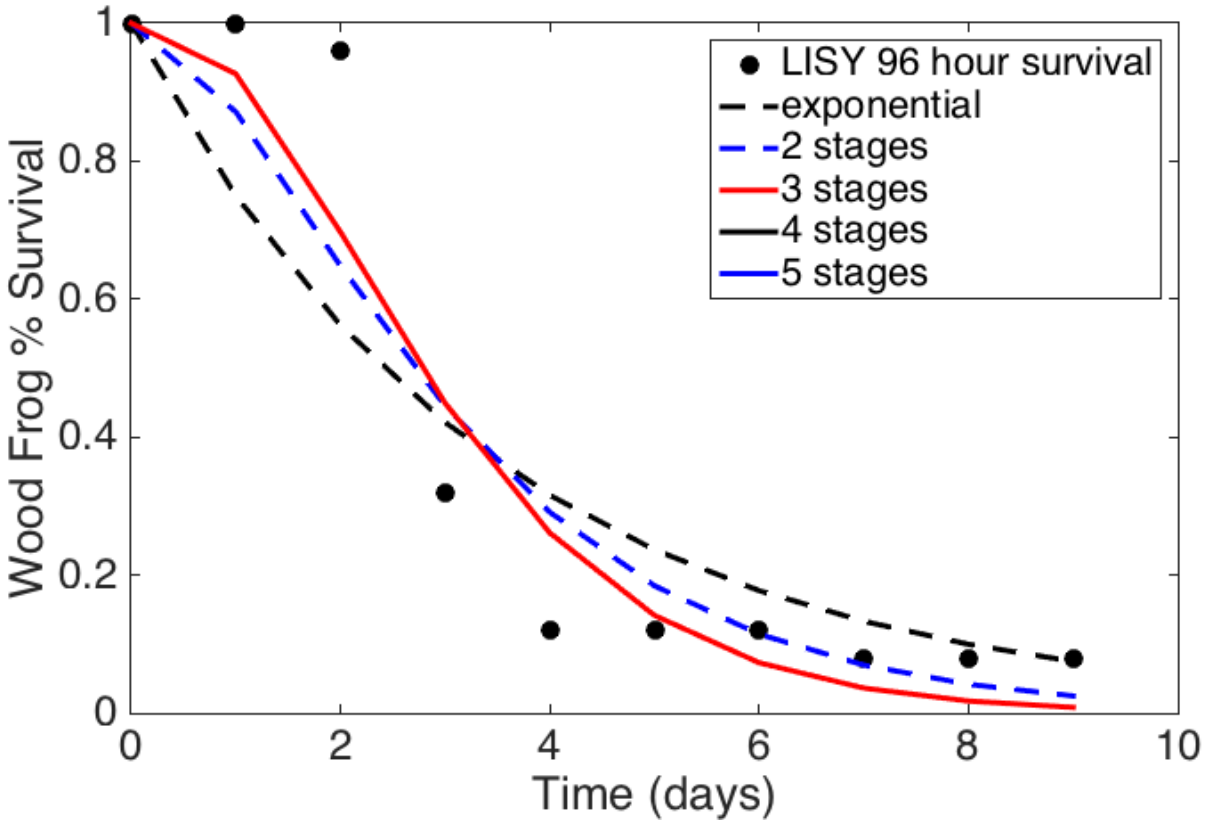

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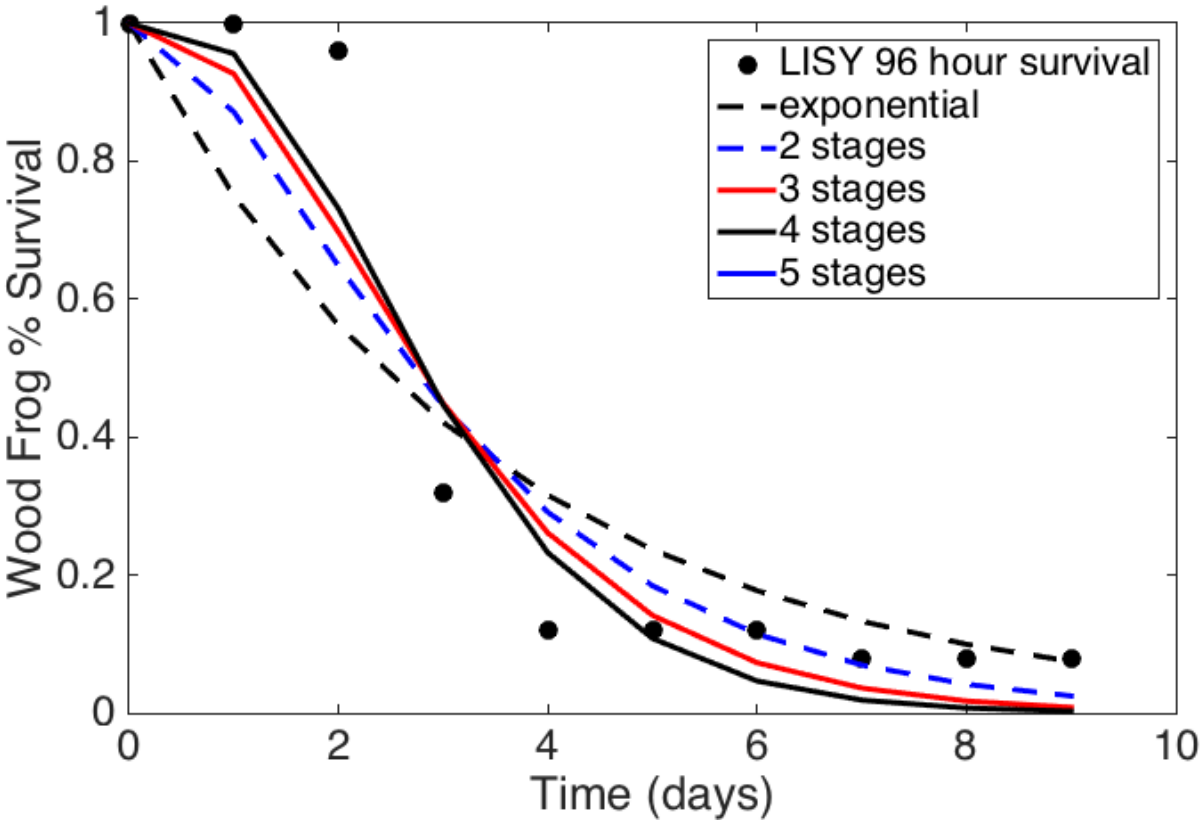

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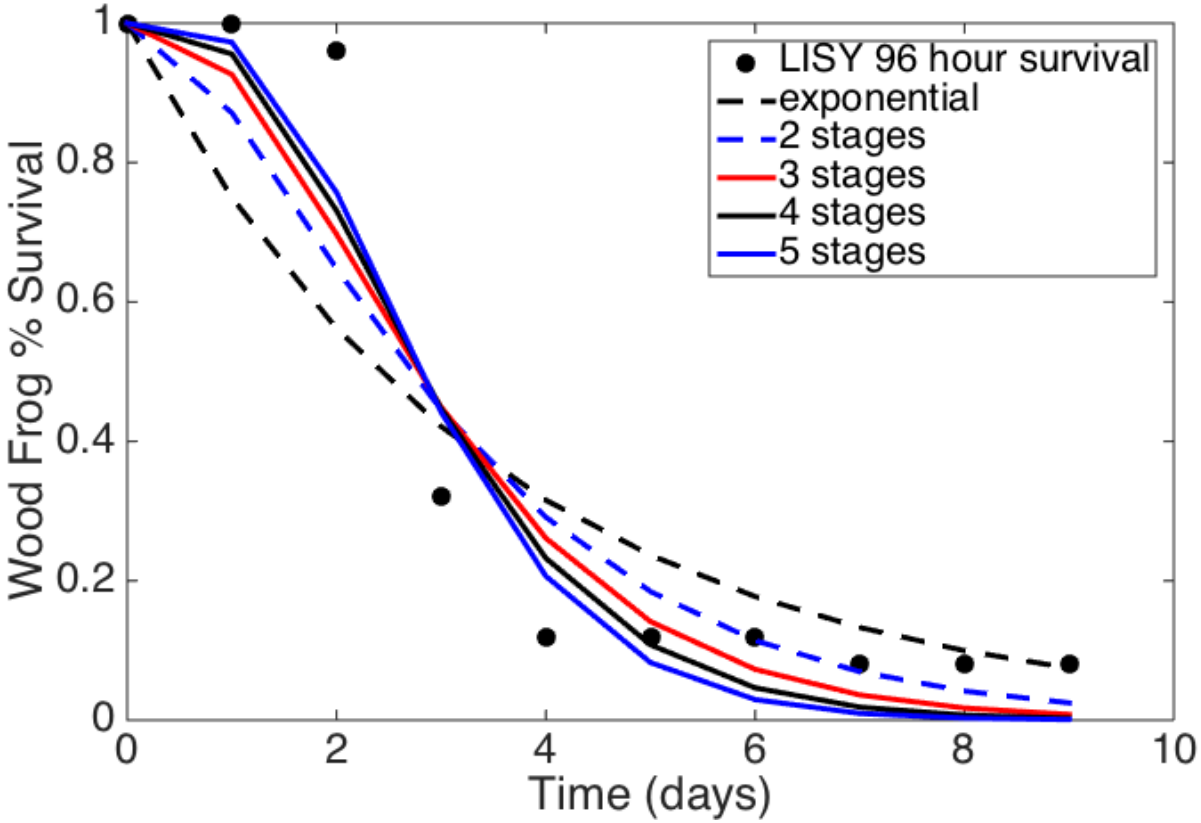
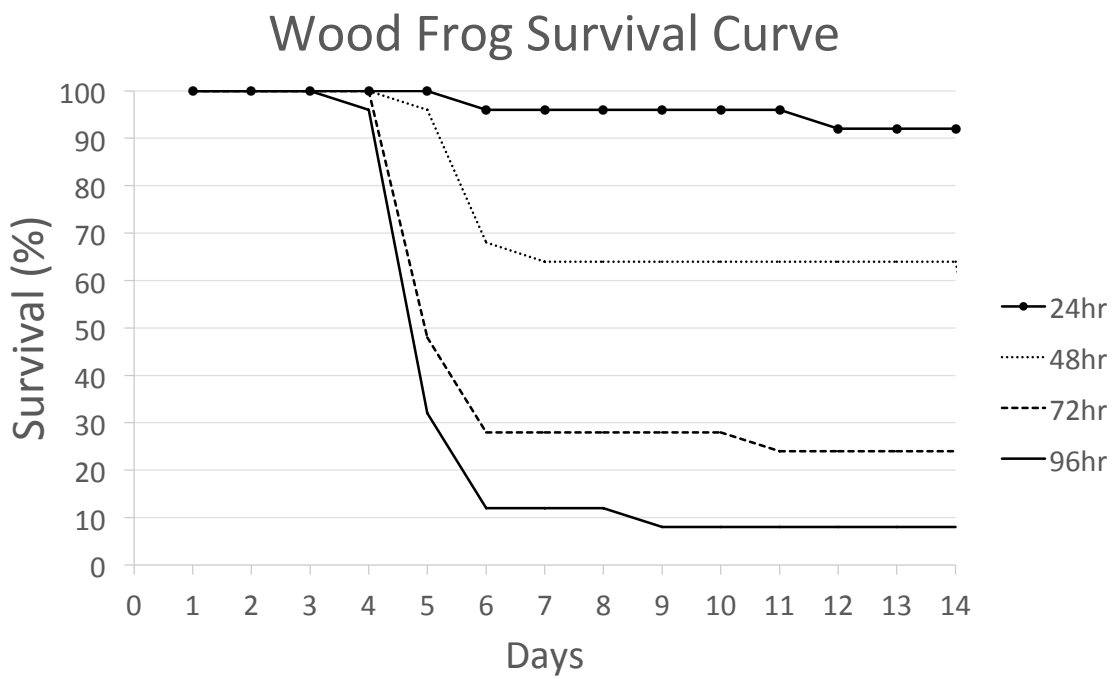


Using 5 stages we get $\mu = 0.3329$ /day

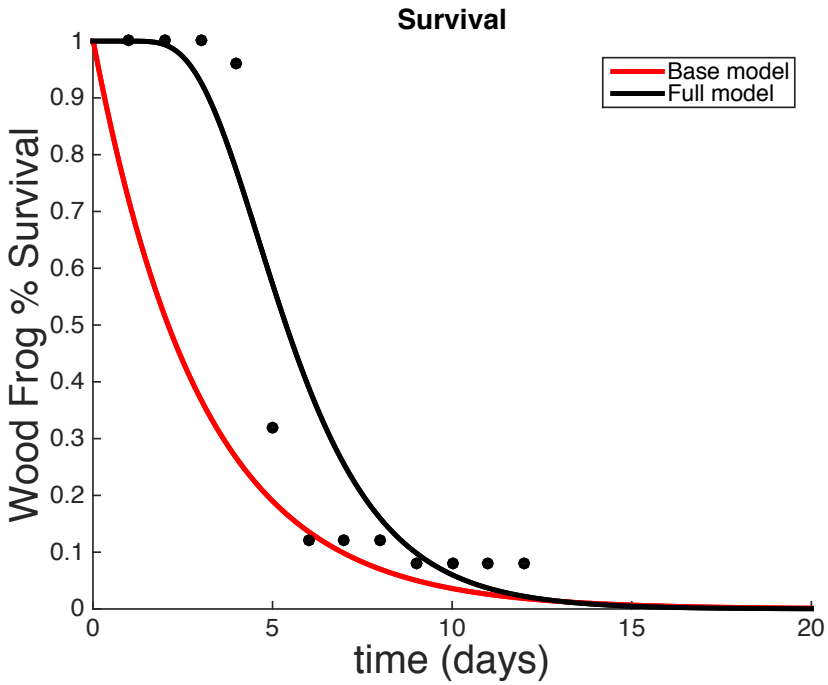
Full Model: Incubation Parameter

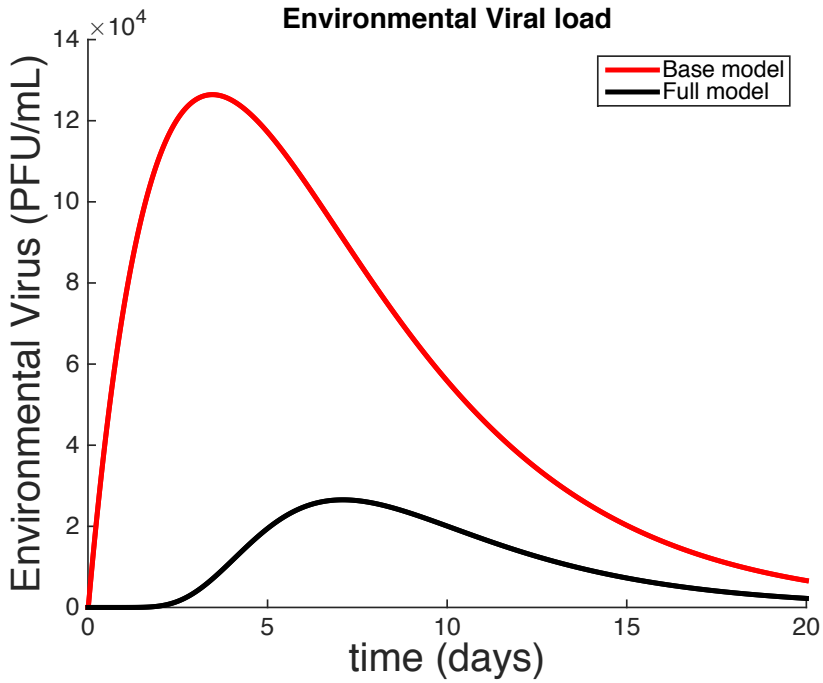
$1/\epsilon$	incubation period



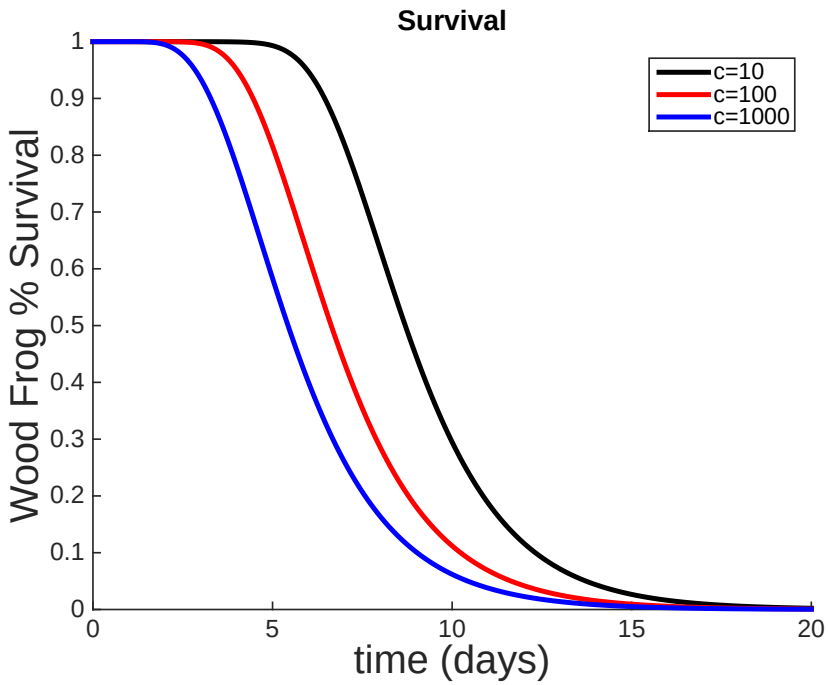
We assume $\frac{1}{\epsilon} = 1$ day

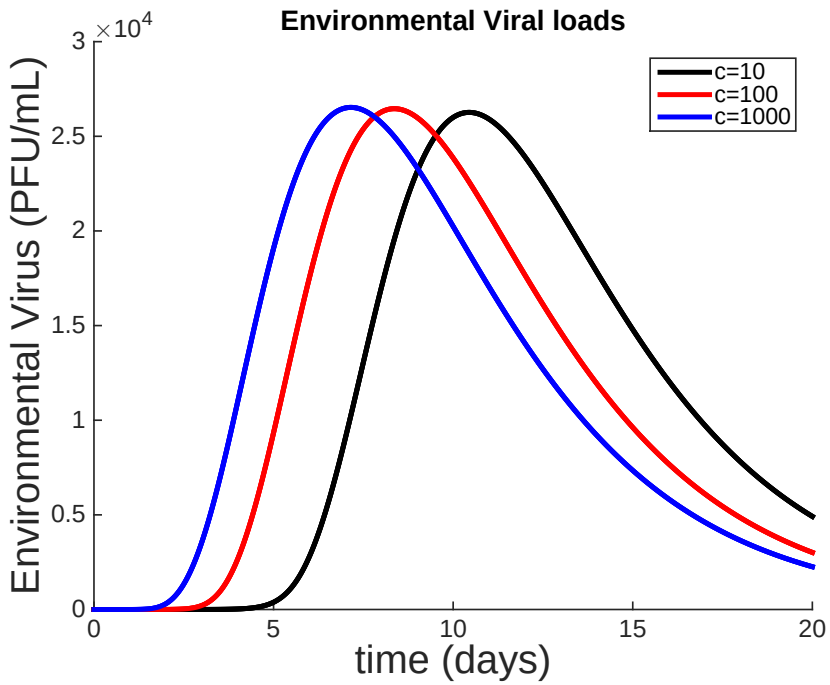
Base vs. Full Model





Full Model Simulations: Vary Contact Rate (density)





Full Model Simulations: Vary Population Size